REMARKS

Claims 1 and 3-18 are pending. Claims 1 and 12 have been amended: to replace "an active agent or agents" with "one or more active agents"; and to remove "and combinations thereof" from the Markush group defining the one or more active agents. "One or more active agents" is the equivalent to "active agent or agents", and the "combination thereof" language is redundant; therefore, the amendments to claims 1 and 12 do not change their scope.

The Abstract has been amended to include the claim limitations that in certain embodiments the emulsion does not contain volatile lower alcohols; and that in certain embodiments the active agent is an anti-inflammatory agent in a concentration of about 0.01% to 10%. As noted by the Examiner, support for these amendments can be found in the claims as originally filed. As required by MPEP § 608.01(b), the Abstract has been also amended to decrease the total number of words to less than 150; specifically, two sentences have been deleted ("In an alternative embodiment, the aqueous phase contains a water-soluble active agent, for example, a local anesthetic, and the oil phase contains a water-insoluble second active agent. The foam is stable on the skin, for example for at least 10 minutes at body temperature, and will disappear into the skin upon rubbing or after prolonged standing.").

No new matter has been added.

Importantly, the claim and specification amendments should not be construed to be an acquiescence to any of the claim rejections or objections to the specification. Rather, the amendments are being made solely to expedite the prosecution of the above-identified application. The Applicants expressly reserve the right to prosecute further the same or similar claims in subsequent patent applications claiming the benefit of priority to the instant application. 35 USC § 120.

RESPONSE TO OBJECTIONS TO THE SPECIFICATION

The Examiner objected to the specification based on the assertion that it lacks disclosure on the recitation of: "the emulsion does not contain volatile lower alcohols does not contain volatile lower alcohols" (claims 1 and 12); and "the concentration of the anti-inflammatory agent

is from about 0.01% to 10%" (claim 5). As noted above, solely to expedite prosecution the Abstract has been amended to recite the above-referenced claim limitations.

In addition, the Examiner suggests that the limitation "an active agent or agents … and combinations thereof" is unclear, suggesting that the claims be re-written as "one or more active agents selected from … and anti-fungal agents." The Applicant appreciates the Examiner's suggestion. As noted above, solely to expedite prosecution, claims 1 and 12 have been amended as suggested by the Examiner.

In light of the amendment to the Abstract, and the amendments to claims 1 and 12, the Applicant respectfully requests withdrawal of the objections to the Specification.

RESPONSE TO CLAIM REJECTIONS MADE UNDER 35 USC § 103(a)

The Examiner contends that claims 1 and 3-18 are unpatentable over Tamarkin 1 (US 2006/0140984) in view of Davis (US 5,143,717), in further view of Sachetto (WO 96/03115). The Examiner further contends that claims 1 and 3-18 are unpatentable over Tamarkin 2 (US 2006/0233721) in view of Quigley, Jr. (US 6,075,056), in further view of Sachetto. The Applicants respectfully traverse.

To establish a *prima facie* case of obviousness, a number of criteria must be met. For example, all of the limitations of a rejected claim must be taught or suggested in the references relied upon by the Examiner; or they must be among the variations that would have been "obvious to try" to one of ordinary skill in the relevant art in light of the cited references. Moreover, one of ordinary skill in the relevant art must have a reasonable expectation of success in light of the combination of cited references. Importantly, the reasonable expectation of success must be found in the prior art, and may not be based on the Applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 U.S.P.Q. 2d 1438 (Fed. Cir. 1991); see MPEP § 2143 - § 2143.03 for decisions pertinent to each of these criteria.

As noted by the Examiner, the combined teaching of Tamarkin 1 and Davis, and the combined teachings of Tamarkin 2 and Quigley, Jr., do not include all of the limitations of the rejected claims because, for example, none of these references discloses a hydrofluoroalkane propellant. The Examiner asserts that this deficiency is cured by Sachetto.

Assuming *arguendo* that all of the limitations of a rejected claim are taught or suggested in the references relied upon by the Examiner, or that any missing limitations are among the variations that would have been "obvious to try," the Applicant respectfully asserts that without the use of lower volatile alcohols there would have been no reasonable expectation of success in using hydrofluorocarbon propellants for immediate foaming compositions.

Sachetto describes aqueous foamable compositions comprising active agents, surfactants and foaming agents. The foaming agents described are liquefied gases, such as propane, butane, isobutene, as well as HFA 134a and HFA 227 (page 4, and table 1). However, the only exemplification provided is for compositions comprising butane as the foaming agent; no compositions comprising HFAs are exemplified, and Sachetto provides no teaching as to why butane and HFAs would reasonably be considered interchangeable.

Moreover, in contrast to the claimed invention, the compositions described by Sachetto feature *delayed* foaming action. Sachetto takes pains to differentiate the disclosed delayed foaming compositions from immediate foaming compositions otherwise known in the art. In this regard, Sachetto teaches away from the using a hydrofluorocarbon propellant for an immediate foaming composition. Pertinently, it is improper to combine references where the references teach away from their combination. *In re Grasselli*, 713 F.2d 731, 743, 218 USPQ 769, 779 (Fed. Cir. 1983). A reference may be said to teach away when a person of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant. One of ordinary skill in the art would have appreciated that the formulations for delayed foaming compositions and immediate foaming compositions are not the same. Therefore, given the guidance provided by Sachetto, one of ordinary skill in the art would not have considered it reasonable to use in an immediate foaming composition a propellant used solely in a delayed foaming composition.

Moreover, in further support of the Applicants' assertion that one of ordinary skill in the art would not have had a reasonable expectation of success based on the art cited by the Examiner, the Applicants direct the Examiner's attention to **Exhibit D** (Smyth, *Advanced Drug Delivery Reviews*, **2003**), and **Exhibit E** (Vervaet, *International Journal of Pharmaceutics,*

1999), which were provided with the Amendment and Response dated December 22, 2009. These articles summarize the difficulties associated with replacing CFC propellants with HFA propellants in aerosol formulations. As explained in Exhibit D, in the paragraph spanning pages 812 and 813:

> Initial screening of alternative propellants identified HFA propellants as likely candidates for replacing CFCs. They appeared to have the necessary physical properties: do not deplete ozone, non-flammable, sufficient vapor pressures, and, importantly, they appeared to be as non-toxic as the CFC counterparts. Although toxicological studies relative to the CFC equivalents that were formulated demonstrated the equivalency of HFAs to CFCs, it was quickly realized that ***HFA propellants were not 'drop in' replacements for CFCs*** in pMDIs. (internal citations omitted; emphasis added)

Remarkably, HFA and CFC propellants differ significantly in their polarities and solubilities in water. In addition, they differ significantly in their ability to dissolve pharmaceutical active ingredients and common pharmaceutical surfactants. Exhibits D and E further explain the then-widespread belief that it was necessary, for example, to incorporate volatile lower alcohols as co-surfactants in order for HFA propellants to function as replacements for CFC propellants. For example, the abstract of Exhibit E explains that:

> [c]onventional (CFC soluble) surfactants are effectively insoluble in the major CFC replacement candidates, HFA 134 and HFA 227ea, in the absence of co-solvents. While these ethane and propane derivatives have comparable boiling points and vapor pressures to dichlorodifluoromethane (CFC 12), their increased polarity demands that formulators use either alternative (soluble) surfactants, or co-solvents along with traditional surfactants, in order to stabilize pressurized suspension products.

In other words, one of ordinary skill in the art would have understood that he or she would not have a reasonable expectation of success in maintaining the operability and efficacy of a CFC-containing formulation upon substituting an HFA for the CFC. Moreover, because the rejected claims specifically require that the formulations "not contain volatile lower alcohols" nor contain "co-solvents or co-propellants" (i.e., the very things which are suggested in the art to make HFA formulations workable as replacements for CFCs), the Applicants respectfully assert that based on the state of the art, as summarized by Exhibits D and E, one of ordinary skill in the art would not have had a reasonable expectation of success in preparing the claimed formulations.

In the Advisory Action mailed January 11, 2010, the Examiner cites the above-quoted paragraph (from Exhibit E) to support the assertion that one of skill in the art would "consider it normal practice to use HFAs in formulations and add or delete co-solvents or surfactants" in order to prepare a stable and desirable formulation. However, the above cited paragraph does not support the Examiner's assertion that one of skill in the art would "delete" co-solvents or surfactants. In fact the paragraph explicitly states the opposite: a formulator would view the use of co-solvents as an absolute necessity when utilizing HFAs. In addition, the authors of Exhibit E explain that the polarity of the HFAs "demands" that when they are used one must also utilize specific soluble surfactants, or traditional surfactants with further co-solvents, in order to obtain a stable product. Consequently, the Applicants respectfully assert that, based on references such as Exhibit E, one of skill in the art would not have had a reasonable expectation of success in preparing the claimed alcohol-free formulations.

Accordingly, the Applicants respectfully request the withdrawal of the claim rejections based on 35 USC § 103(a).

FEES

The Applicants believe that all of the fees required in connection with the filing (i.e., the fee for a one month extension of time) of this paper have been provided. Nevertheless, the Director is hereby authorized to charge any additional required fee(s) to our Deposit Account, **06-1448**, reference **CPX-015.01**.

CONCLUSION

In view of the above remarks, the Applicants believe that the pending claims are in condition for allowance. If a telephone conversation would expedite prosecution of the application, the Examiner is urged to contact the undersigned.

Respectfully submitted,

FOLEY HOAG LLP

/Jacob I. Wasserman/

Jacob I. Wasserman, Ph.D.
Attorney for Applicants
Registration No. 56,929

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Patent Group
FOLEY HOAG LLP

155 Seaport Boulevard
Boston, MA 02210

617-832-1000
617-832-7000 (FAX)